HPS Trailer Page for

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Summary

Document	Pages	Printed	Missed
US005681728	. 16	16	0
Total (1)	16	16	0

H W	······································		
Err	0	0	0
Error Definition			
Comments			
Time Stamp	2001/05/16 07:41	2001/05/16 07:41	2001/05/16 07:43
DBs 1	USPAT; US-PGP UB; EPO; JPO; DERWEN T; IBM	USPAT; US-PGP UB; EPO; JPO; DERWEN T; IBM	USPAT; US-PGP US: UB; OP Or JPO; OT T; IBM T; IBM
Search Text	((hyaluron\$4 or acp or luronit or mucoitin) near2 ester) or hyaff	((hyaluron\$4 or acp or luronit or mucoitin) near5 ester) or hyaff	((osteogenic or bone protein) or bmp or o op-1 or op1 or bone
Hits	241	321	136541
T #	L 1	L2	L3
Type	BRS	BRS	
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Error Definition			
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DBs	USPAT; US-PGP UB; EPO; JPO; DERWEN T; IBM	USPAT; US-PGP UB; EPO; JPO; DERWEN T; IBM	
Search Text	12 and 13	12 same 13	
Hits	85	13	
#	1.4	L.5	
Type	BRS	BRS	
	4	ري د	

```
ANSWER 1 OF 1 REGISTRY COPYRIGHT 2001 ACS
L1
     129805-33-0 REGISTRY
RN
     Bone morphogenetic protein 7, prepro- (human clone HH(dT+R)-1 reduced)
CN
     (9CI)
            (CA INDEX NAME)
OTHER NAMES:
     11: PN: WO0066620 SEQID: 2 unclaimed protein
CN
     1: PN: WO0029012 SEQID: 2 claimed protein
CN
     2: PN: WO0123563 SEQID: 2 unclaimed protein
CN
     34: PN: WO0020449 SEQID: 39 unclaimed protein
CN
     38: PN: WO0020607 SEQID: 39 claimed protein
CN
     39: PN: WO0020591 SEQID: 39 claimed protein
CN
     3: PN: US6110482 SEQID: 2 unclaimed protein
CN
     3: PN: WO0066620 SEQID: 3 claimed protein
CN
     7: PN: WO0020021 SEQID: 2 unclaimed protein
CN
     Bone morphogenetic protein 7 (human precursor)
CN
     Bone morphogenetic protein 7 (human)
CN
     Bone morphogenetic protein 7, prepro- (human)
CN
     Glycoprotein (human clone PEH7-9 bone morphogenetic 7 subunit precursor
CN
     protein moiety reduced)
     Glycoprotein OP 1, prepro- (human clone HH(dT+R)-1 osteogenic protein
CN
     moiety reduced)
CN
     Glycoprotein, prepro- (human clone morphogenetic 7 subunit protein moiety
     reduced)
CN
     OP-1 (human)
     Osteogenic protein 1 (human)
CN
     osteogenic protein X, prepro- (human)
CN
     Protein OP 1 (human brain osteogenic)
CN
     Protein OP-1 (human osteogenic protein-1)
CN
     PROTEIN SEQUENCE
FS
     133606-73-2, 134548-31-5, 199945-19-2
DR
MF
     Unspecified
CI
     MAN
SR
     CA
     STN Files: CA, CAPLUS, TOXLIT, USPATFULL
LC
*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
*** USE 'SQD' OR 'SQIDE' FORMATS TO DISPLAY SEQUENCE ***
              23 REFERENCES IN FILE CA (1967 TO DATE)
               2 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
```

22 REFERENCES IN FILE CAPLUS (1967 TO DATE)

ANSWER 1 OF 3 REGISTRY COPYRIGHT 2001 ACS 186378-26-7 REGISTRY RN CN Glycine, L-valyl-L-prolyl-L-threonyl-L-.alpha.-glutamyl-L-leucyl-L-seryl-Lalanyl-L-isoleucyl-L-seryl-L-methionyl-L-leucyl-L-tyrosyl-L-leucyl-L-.alpha.-aspartyl-L-.alpha.-glutamyl-L-asparaginyl-L-.alpha.-glutamyl-Llysyl-L-valyl-L-leucyl-L-lysyl-L-asparaginyl-L-tyrosyl-Lglutaminyl-L-.alpha.-aspartyl-L-methionyl-L-valyl-L-valyl-L-.alpha.glutamyl- (9CI) (CA INDEX NAME) OTHER NAMES: CN BMP-2A (human finger 2 domain-contg. fragment) PROTEIN SEQUENCE; STEREOSEARCH FS MF C156 H252 N36 O52 S2 SR CA LCCA, CAPLUS, TOXLIT, USPATFULL STN Files:

Absolute stereochemistry.

PAGE 1-A

PAGE 1-B

PAGE 1-D

- 1 REFERENCES IN FILE CA (1967 TO DATE)
 1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
 1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

```
ANSWER 1 OF 1 REGISTRY COPYRIGHT 2001 ACS
     9004-61-9 REGISTRY
     Hyaluronic acid (8CI, 9CI) (CA INDEX NAME)
OTHER NAMES:
     ACP
     ACP (polysaccharide)
    ACP gel
    Hyaluronan
CN
    Luronit
CN
    Mucoitin
CN
     Sepracoat
     9039-38-7, 37243-73-5, 29382-75-0
DR
MF
     Unspecified
CI
     PMS, COM, MAN
PCT Manual registration, Polyester, Polyester formed
     STN Files: ADISINSIGHT, AGRICOLA, ANABSTR, BIOBUSINESS, BIOSIS,
       BIOTECHNO, CA, CABA, CANCERLIT, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS,
       CHEMLIST, CIN, CSCHEM, DDFU, DRUGNL, DRUGU, DRUGUPDATES, EMBASE,
IFICDB,
       IFIPAT, IFIUDB, IMSDIRECTORY, IPA, MEDLINE, MRCK*, NAPRALERT, NIOSHTIC,
       PHAR, PIRA, PROMT, TOXLINE, TOXLIT, USAN, USPATFULL
         (*File contains numerically searchable property data)
     Other Sources: DSL**, EINECS**, TSCA**
         (**Enter CHEMLIST File for up-to-date regulatory information)
*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
            7606 REFERENCES IN FILE CA (1967 TO DATE)
            568 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
```

7614 REFERENCES IN FILE CAPLUS (1967 TO DATE)

```
ANSWER 1 OF 1 REGISTRY COPYRIGHT 2001 ACS
     7758-87-4 REGISTRY
     Phosphoric acid, calcium salt (2:3) (8CI, 9CI) (CA INDEX NAME)
OTHER NAMES:
     .alpha.-Tricalcium phosphate
CN
     .beta.-TCP
CN
     .beta.-Tricalcium phosphate
CN
     .beta.-Whitlockite
CN
     Apamicron AP 12C
CN
     Bonarka
CN
     Calcium orthophosphate
CN
    Calcium orthophosphate (Ca3(PO4)2)
    Calcium phosphate
CN
CN
    Calcium phosphate (3:2)
CN
     Calcium phosphate (Ca3(PO4)2)
CN
     Calcium tertiary phosphate
CN
     Multifos
CN
     Phosphoric acid calcium(2+) salt (2:3)
CN
     Posture
CN
     Posture (calcium supplement)
CN
     Synthograft
CN
     Synthos
CN
     TCP
CN
     TCP 10
CN
     Tertiary calcium phosphate
CN
     Tribasic calcium phosphate
CN
     Tricalcium diphosphate
CN
     Tricalcium orthophosphate
CN
     Tricalcium phosphate
CN
     Tricalcium phosphate (Ca3(PO4)2)
     1344-15-6, 123211-19-8
DR
ΜF
     Ca . 2/3 H3 O4 P
CI
     COM
                  AGRICOLA, ANABSTR, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CABA,
LC
       CANCERLIT, CAOLD, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CHEMLIST, CIN,
       CSCHEM, DDFU, DETHERM*, DIOGENES, DRUGU, EMBASE, GMELIN*, HSDB*,
IFICDB,
       IFIPAT, IFIUDB, MEDLINE, MRCK*, MSDS-OHS, NIOSHTIC, PDLCOM*, PHAR.
PIŖA,
       PROMT, TOXLINE, TOXLIT, TULSA, USPATFULL, VETU, VTB
         (*File contains numerically searchable property data)
                      DSL**, EINECS**, TSCA**
         (**Enter CHEMLIST File for up-to-date regulatory information)
CRN (7664-38-2)
   0
HO- P- OH
   OH
```

• 3/2 Ca

L6 ANSWER 1 OF 9 REGISTRY COPYRIGHT 2001 ACS

RN 186378-43-8 REGISTRY

CN L-Isoleucine,

L-phenylalanyl-L-.alpha.-aspartyl-L-.alpha.-aspartyl-L-seryl-L-seryl-L-seryl-L-asparaginyl-L-valyl- (9CI) (CA INDEX NAME)
OTHER NAMES:

CN OP-1 (human finger 2 domain small peptide-contg. fragment)

FS PROTEIN SEQUENCE; STEREOSEARCH

MF C38 H57 N9 O16

SR CA

LC STN Files: CA, CAPLUS, TOXLIT, USPATFULL

Absolute stereochemistry.

- 1 REFERENCES IN FILE CA (1967 TO DATE)
- 1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
- 1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

Trying 3106016892...Open

NEWS 1

NEWS WWW

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TSCA INFORMATION NOW CURRENT THROUGH January 11, 2001

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Structure search limits have been increased. See HELP SLIMIT for details.

```
=> e bmp/cn
E1
             1
                    BMNO/CN
E2
             1
                    BMOO/CN
             2
E3
               --> BMP/CN
E4
             1
                    BMP (CORROSION INHIBITOR)/CN
                    BMP (PEPTIDE)/CN
E5
             1
             1
                   BMP 1/CN
E6
E7
             1
                   BMP 10 (MOUSE GENE BMP10 PRECURSOR)/CN
E8
             1
                   BMP 10 (MOUSE GENE BMP10)/CN
                   BMP 2/CN
E9
             1
                   BMP 3/CN
E10
             1
E11
             1
                   BMP 4/CN
E12
                   BMP RECEPTOR IB (DANIO RERIO STRAIN AB)/CN
=> s e5
             1 "BMP (PEPTIDE)"/CN
L1
=> d 11
L1
     ANSWER 1 OF 1 REGISTRY COPYRIGHT 2001 ACS
     73984-05-1 REGISTRY
RN
     L-Alanine, L-lysylglycyl-L-.alpha.-aspartyl-L-.alpha.-glutamyl-L-.alpha.-
CN
     glutamyl-L-seryl-L-leucyl- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
     L-Alanine, N-[N-[N-[N-[N-[N-(N-L-lysylglycyl)-L-.alpha.-aspartyl]-L-
     .alpha.-glutamyl]-L-.alpha.-glutamyl]-L-seryl]-L-leucyl]-
OTHER NAMES:
CN
     242: PN: WO0069900 SEQID: 1546 unclaimed sequence
```

CN BMP

CN BMP (peptide)

CN Delicious peptide

FS PROTEIN SEQUENCE; STEREOSEARCH

MF C34 H57 N9 O16

LC STN Files: AGRICOLA, BIOBUSINESS, CA, CAPLUS, CHEMCATS, TOXLIT

Absolute stereochemistry.

22 REFERENCES IN FILE CA (1967 TO DATE)

1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA

22 REFERENCES IN FILE CAPLUS (1967 TO DATE)

=> d 11

L1 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2001 ACS

RN 73984-05-1 REGISTRY

CN L-Alanine, L-lysylglycyl-L-.alpha.-aspartyl-L-.alpha.-glutamyl-L-.alpha.-glutamyl-L-seryl-L-leucyl- (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN L-Alanine, N-[N-[N-[N-[N-(N-L-lysylglycyl)-L-.alpha.-aspartyl]-L-.alpha.-glutamyl]-L-.alpha.-glutamyl]-L-seryl]-L-leucyl]-OTHER NAMES:

CN 242: PN: WO0069900 SEQID: 1546 unclaimed sequence

CN BMP

CN BMP (peptide)

CN Delicious peptide

FS PROTEIN SEQUENCE; STEREOSEARCH

MF C34 H57 N9 O16

LC STN Files: AGRICOLA, BIOBUSINESS, CA, CAPLUS, CHEMCATS, TOXLIT

Absolute stereochemistry.

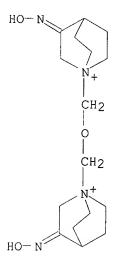
PAGE 1-B

22 REFERENCES IN FILE CA (1967 TO DATE)

1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA

22 REFERENCES IN FILE CAPLUS (1967 TO DATE)

```
' E1
              1
                    BMP 10 (MOUSE GENE BMP10 PRECURSOR)/CN
 E2
              1
                    BMP 10 (MOUSE GENE BMP10)/CN
 E3
              1 --> BMP 2/CN
 E4
              1
                   BMP 3/CN
 E5
                   BMP 4/CN
              1
                   BMP RECEPTOR IB (DANIO RERIO STRAIN AB)/CN
 Ε6
              1
 E7
             1
                   BMP RECEPTOR KINASE-1/CN
 E8
             1
                   BMP RECEPTOR KINASE-2/CN
 Ε9
                   BMP RECEPTOR KINASE-3/CN
             1
                   BMP TYPE II RECEPTOR (XENOPUS LAEVIS CLONE C6 GENE
              1
 E10
 XBMPR-II)
                   /CN
 E11
                   BMP-2A (CATTLE CLONE .LAMBDA.BP-21 REDUCED)/CN
                   BMP-2A (HUMAN FINGER 1 DOMAIN-CONTG. FRAGMENT)/CN
 E12
 => s e3
 L2
             1 "BMP 2"/CN
 => d 12
     ANSWER 1 OF 1 REGISTRY COPYRIGHT 2001 ACS
     192509-82-3 REGISTRY
    1-Azoniabicyclo[2.2.2]octane,
 1,1'-[oxybis(methylene)]bis[3-(hydroxyimino)-
     , diiodide (9CI) (CA INDEX NAME)
 OTHER NAMES:
CN
     BMP 2
MF
     C16 H28 N4 O3 . 2 I
SR
    STN Files: ADISINSIGHT, BIOSIS, CA, CAPLUS, TOXLIT
LC
```



• 2 I-

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

=> e bmp-2/cn

```
E.1
                         1 BMP RECEPTOR KINASE-3/CN
 E2
                       1
                                 BMP TYPE II RECEPTOR (XENOPUS LAEVIS CLONE C6 GENE
 XBMPR-II)
                                    /CN
                         0 --> BMP-2/CN
                  U --> BMP-2/CN

BMP-2A (CATTLE CLONE .LAMBDA.BP-21 REDUCED)/CN

BMP-2A (HUMAN FINGER 1 DOMAIN-CONTG. FRAGMENT)/CN

BMP-2A (HUMAN FINGER 2 DOMAIN-CONTG. FRAGMENT)/CN

BMP-2A (HUMAN HEEL DOMAIN-CONTG. FRAGMENT)/CN

BMP-3 (HUMAN FINGER 1 DOMAIN-CONTG. FRAGMENT)/CN

BMP-3 (HUMAN FINGER 2 DOMAIN-CONTG. FRAGMENT)/CN

BMP-3 (HUMAN FINGER 2 DOMAIN-CONTG. FRAGMENT)/CN

BMP-4 (HUMAN FINGER 1 DOMAIN-CONTG. FRAGMENT)/CN

BMP-4 (HUMAN FINGER 2 DOMAIN-CONTG. FRAGMENT)/CN
 E7
 E8
 E9
 E10
 E11
 E12
 => s e5
                        1 "BMP-2A (HUMAN FINGER 1 DOMAIN-CONTG. FRAGMENT)"/CN
 L3
 => e hyaluronic/cn
                                 HYALURONATE SYNTHASE PXO1-93 (BACILLUS ANTHRACIS STRAIN
 STER
                                  NE PLASMID PXO1)/CN
                                 HYALURONATE SYNTHETASE/CN
                        0 --> HYALURONIC/CN
                  HYALURONIC ACID/CN

HYALURONIC ACID/CN

HYALURONIC ACID .BETA.-PHENYLETHYL ESTER/CN

HYALURONIC ACID 2,6-DICHLOROBENZYL ESTER/CN

HYALURONIC ACID 3,4,5-TRIMETHOXYBENZYL ESTER/CN

HYALURONIC ACID 4-TERBUTYLBENZYL ESTER/CN

HYALURONIC ACID BENZYL ARACHIDYL ESTER/CN

HYALURONIC ACID BENZYL DOCOSANYL ESTER/CN

HYALURONIC ACID BENZYL ESTER/CN

HYALURONIC ACID BENZYL ESTER/CN
 E7
 E8
 E9
 E10
 E11
E12
=> s e4
            1 "HYALURONIC ACID"/CN
T.4
=> s phosphate/cn
L5
                       1 PHOSPHATE/CN
=> e phosphate/cn
E1
                                   PHOSPHATASE/KINASE (CHLAMYDIA PNEUMONIAE STRAIN J138 GENE
YΑ
                                   CE)/CN
E2
                                  PHOSPHATASE/KINASE (CHLAMYDIA TRACHOMATIS GENE YACE)/CN
                        1 --> PHOSPHATE/CN
E3
               PHOSPHATE/CN

PHOSPHATE (32PO4)/CN

PHOSPHATE (H2PO4-)/CN

PHOSPHATE (H2PO41-)/CN

PHOSPHATE (HPO42-)/CN

PHOSPHATE (P2O74-)/CN

PHOSPHATE (P4O123-)/CN

PHOSPHATE (P4O136-), (OC-6-11)-HEXAAMMINECOBALT(3+)
E4
E5
Ε6
E7
Ε8
Ε9
E10
(1:2)/CN
                      1 PHOSPHATE (P40136-), (OC-6-11)-HEXAAMMINECOBALT(3+) (1:2),
E11
Т
                                 RIHYDRATE/CN
                              PHOSPHATE (P50143-)/CN
E12
                       1
=> d 15
```

```
, F2
       ANSWER 1 OF 1 REGISTRY COPYRIGHT 2001 ACS
       14265-44-2 REGISTRY
       Phosphate (8CI, 9CI) (CA INDEX NAME)
 OTHER NAMES:
       Orthophosphate
 CN
 CN
       Orthophosphate (PO43-)
 CN
       Orthophosphate (3-)
 CN
       Phosphate (PO43-)
 CN
       Phosphate anion(3-)
 CN
       Phosphate ion (PO43-)
 CN
       Phosphate ion(3-)
 CN
       Phosphate trianion
 CN
       Phosphate (3-)
 CN
       Phosphoric acid, ion(3-)
 FS
       3D CONCORD
 DR
       264888-19-9
 ΜF
       04 P
 CI
       COM
 LC
       STN Files: AGRICOLA, ANABSTR, BIOBUSINESS, BIOSIS, BIOTECHNO, CA,
         CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CHEMLIST, CIN, CSCHEM, CSNB, DDFU, DRUGU, EMBASE, GMELIN*, IFICDB, IFIPAT, IFIUDB, IPA, NIOSHTIC, PIRA, PROMT, TOXLINE, TOXLIT, TULSA, ULIDAT, USPATFULL, VETU, VTB
           (*File contains numerically searchable property data)
       Other Sources: NDSL**, TSCA**
            (**Enter CHEMLIST File for up-to-date regulatory information)
     \bigcirc
  O- P- O-
     0-
             30877 REFERENCES IN FILE CA (1967 TO DATE)
                254 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
             30896 REFERENCES IN FILE CAPLUS (1967 TO DATE)
 => f .genbiotech toxlit txline
               0 GENBIOTECH
               0 TOXLIT
               0 TXLINE
 L6
               O .GENBIOTECH TOXLIT TXLINE
                    (GENBIOTECH (W) TOXLIT (W) TXLINE)
 => f .genbiotech toxlit toxline
               0 GENBIOTECH
               0 TOXLIT
               0 TOXLINE
L7
               O .GENBIOTECH TOXLIT TOXLINE
                    (GENBIOTECH (W) TOXLIT (W) TOXLINE)
=> fil .genbiotech toxlit toxline
COST IN U.S. DOLLARS
                                                         SINCE FILE
                                                                           TOTAL
                                                              ENTRY
                                                                         SESSION
FULL ESTIMATED COST
                                                              50.90
                                                                           51.20
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 FILE 'TOXLINE' ENTERED AT 14:56:06 ON 14 MAY 2001
 => s 13 or ((osteogenic or bone) (2a) protein) or bmp or op or op-1 or op1
    3 FILES SEARCHED...
    6 FILES SEARCHED...
    8 FILES SEARCHED...
          63570 L3 OR ((OSTEOGENIC OR BONE) (2A) PROTEIN) OR BMP OR OP OR OP-1
                OR OP1
 => s 14 or hyaluron? or acp or luronit or mucoitin
    8 FILES SEARCHED...
         79048 L4 OR HYALURON? OR ACP OR LURONIT OR MUCOITIN
 => s 15 or orthophosphate or phosphate or phosphoric
    7 FILES SEARCHED...
     1229074 L5 OR ORTHOPHOSPHATE OR PHOSPHATE OR PHOSPHORIC
=> s 18 and 19 and 110
L11
            38 L8 AND L9 AND L10
=> dup rem 111
PROCESSING COMPLETED FOR L11
             32 DUP REM L11 (6 DUPLICATES REMOVED)
=> s 112 bib abs 1-
MISSING OPERATOR L12 BIB
The search profile that was entered contains terms or
nested terms that are not separated by a logical operator.
=> d 112 bib abs 1-
YOU HAVE REQUESTED DATA FROM 32 ANSWERS - CONTINUE? Y/(N):y
L12 ANSWER 1 OF 32 CAPLUS COPYRIGHT 2001 ACS
     2001:300558 CAPLUS
    134:300839
TI
     Formulations of hyaluronic acid for delivery of
     osteogenic proteins
```

```
Kim, Hyun; Li, Rebecca; Pavesio, Alessandra; Callegaro, Lanfranco
     Genetics Institute, Inc., USA; Fidia Advanced Biology
SO
     PCT Int. Appl., 20 pp.
     CODEN: PIXXD2
DT
     Patent
LA
     English
FAN.CNT 1
     PATENT NO.
                  KIND DATE
                                          APPLICATION NO. DATE
                                           ______
     WO 2001028602 A1 20010426 WO 2000-US28468 20001013
PΤ
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             CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR,
             HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT,
             LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU,
             SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU,
             ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
             DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
PRAI US 1999-159674
                      Ρ
                            19991015
     US 2000-185587
                      Ρ
                            20000228
AΒ
     An injectable formulation is disclosed for delivery of osteogenic
     proteins. The formulation comprises a pharmaceutically acceptable
     admixt. of an osteogenic protein; and formulations
     comprising osteogenic protein, hyaluronic
     acid derivs. and tricalcium phosphate are also disclosed.
     Methods for formulating porous injectable gels and pastes from
     hyaluronic acid are also disclosed. Hyaff-11p80 was solubilized
     in N-methylpyrrolidinone, then mixed with RhBMP-2-contg. buffer (0.1
     mg/mL) followed by addn. of various pore formers (like sodium
bicarbonate)
     and tricalcium phosphate. In vitro release kinetics of the
     rhBMP-2 was studied.
RE.CNT 6
RE
(1) Callegaro, L; WO 9320858 A 1993 CAPLUS
(2) Callegaro, L; WO 9749412 A 1997 CAPLUS
(3) Callegaro, L; WO 9924070 A 1999 CAPLUS
(5) Univ Brown Res Found; WO 9745532 A 1997 CAPLUS
(6) Univ Florida; WO 9117777 A 1991 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT
L12 ANSWER 2 OF 32 WPIDS COPYRIGHT 2001
                                            DERWENT INFORMATION LTD
AN
     2001-202687 [20] WPIDS
DNN
    N2001-144640
                       DNC C2001-060149
TΙ
     Delivery of agents into targeted tissue, particularly cardiac tissue
     comprises a flowable substance containing a number of small particles.
DC
     A96 B05 B07 P31
ΙN
     EVANS, D G; HOGANSON, D M; NASH, J E
PΑ
     (KENS-N) KENSEY NASH CORP
CYC 94
ΡI
     WO 2001010313 A1 20010215 (200120)* EN
        RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ
            NL OA PT SD SE SL SZ TZ UG ZW
        W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM
            DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC
           LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE
            SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
    WO 2001010313 A1 WO 2000-US20525 20000728
PRAI US 1999-368410 19990805
    2001-202687 [20] WPIDS
    WO 200110313 A UPAB: 20010410
    NOVELTY - A system (I) for delivering agents into a targeted internal
    tissue comprising a delivery instrument (II) and a flowable agent (III)
    containing a number of small particles for introduction into the tissue,
    where (II) is arranged to introduce (III) at or adjacent the tissue by
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imparting a force to (III) which enters the tissue at an entry sinus, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for (I) for vascularizing cardiac tissue to cause the formation of lumens in communication with the patient's arterial system and treating cardiac tissue to affect the conduction of electrical signals or nerve signals in the cardiac tissue.

 $\ensuremath{\mathsf{USE}}$ - For delivering agents into targeted tissue, particularly cardiac tissue (claimed).

ADVANTAGE - The local intra-tissue delivery of the flowable agent is more efficient than previous systems for delivery of medications to the heart, i.e. systemically by vein or regionally, e.g. intracoronary infusion.

Dwg.0/22

L12 ANSWER 3 OF 32 TOXLIT

AN 2001:15957 TOXLIT

DN CA-134-300839W

TI Formulations of hyaluronic acid for delivery of osteogenic proteins.

AU Kim H; Li R; Pavesio A; Callegaro L

SO (2001). PCT Int. Appl. PATENT NO. 0128602 04/26/2001 (Fidia Advanced Biology).

CODEN: PIXXD2.

CY UNITED STATES

DT Patent

FS CA

LA English

OS CA 134:300839

EM 200105

AB An injectable formulation is disclosed for delivery of osteogenic proteins. The formulation comprises a pharmaceutically acceptable admixt. of an osteogenic protein; and formulations comprising osteogenic protein, hyaluronic acid derivs. and tricalcium phosphate are also disclosed. Methods for formulating porous injectable gels and pastes from hyaluronic acid are also disclosed. Hyaff-1lp80 was solubilized in N-methylpyrrolidinone, then mixed with RhBMP-2-contg. buffer (0.1 mg/mL) followed by addn. of various pore formers (like sodium bicarbonate) and tricalcium phosphate. In vitro release kinetics of the rhBMP-2 was studied.

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L12 ANSWER 4 OF 32 CAPLUS COPYRIGHT 2001 ACS DUPLICATE 1
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AN 2000:880973 CAPLUS

DN 134:33046

TI Bone graft substitute composition containing calcium sulfate

IN Petersen, Don; Haggard, Warren O.; Randolph, Don; Hagan, Carv

PA Wright Medical Technology, Inc., USA

SO PCT Int. Appl., 20 pp. CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

PΙ

W: AU, CA, JP

RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE

PRAI US 1999-327761 A 19990607

AB A bone graft substitute compn. comprising calcium sulfate; a mixing soln. selected from the group consisting of sterile water, sodium chloride, phosphate buffered saline, potassium chloride, and sodium sulfate; and a plasticizing substance selected from the group consisting of CM-cellulose, polyvinyl alc., Me cellulose, and hydroxypropyl Me cellulose. For example, an injectable bone graft substance compn. was

prepd. contg. (by wt.) 100 parts of CaSO4 (as hemihydrate), 11.1 parts of CM-cellulose, 69.4 parts of demineralized bone matrix, and 162 parts of sterile water. The compn. was well tolerated by the bone and healed a large medullary defect 30-100% at 6 wk with viable new bone in a canine model. RE.CNT 3 (1) Biocoll Laboratories Inc; WO 9639203 Al 1996 CAPLUS (2) O'Leary; US 5484601 A 1996 (3) Yim; US 5385887 A 1995 CAPLUS L12 ANSWER 5 OF 32 CAPLUS COPYRIGHT 2001 ACS DUPLICATE 2 2000:861445 CAPLUS DN 134:21514 Implant for application in bone, method for producing such an implant, TIuse of such an implant INHall, Jan Nobel Biocare AB (Publ), Swed. PCT Int. Appl., 26 pp. CODEN: PIXXD2 DTPatent LA English FAN.CNT 1 PATENT NO. KIND DATE APPLICATION NO. DATE ____ ----------WO 2000072775 A1 20001207 WO 2000-SE1022 20000519 W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG SE 9901973 · A 20001201 SE 1999-1973 19990531 PRAI SE 1999-1973 Α 19990531 AB An implant for application in bone, for example the jaw bone, primarily the human body, comprises a unit which can be applied in the bone in question and which is made of biocompatible material, preferably titanium. On its surface parts cooperating with the bone, the unit is provided with a coating (or coatings) of an agent (substance) TS, which initiates stimulates bone growth. The coating (or coatings) comprises (comprise) calcium phosphate compds. CaP and the said stimulating agent TS. RE.CNT 3 (1) Matrix Medical B V; EP 0806212 A1 1997 CAPLUS (2) Nobel Biocare Ab; WO 9848862 Al 1998 CAPLUS (3) Per, I; US 4330891 A 1982 L12 ANSWER 6 OF 32 CAPLUS COPYRIGHT 2001 ACS DUPLICATE 3 2000:84661 CAPLUS 132:127773 Calcium phosphate and biopolymer for bone reconstruction Larsson, Cecilia; Ljusberg-wahren, Helena Nobel Biocare Ab (Publ), Swed.; Gs Development Ab PCT Int. Appl., 34 pp. CODEN: PIXXD2 Patent English FAN.CNT 1

APPLICATION NO. DATE

PΤ

of

AN DN

TΙ

ΙN

PΑ

SO

DT

LA

PATENT NO.

KIND DATE

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, PI
      WO 2000004940
                     A1 20000203
                                          WO 1999-SE1231 19990706
          W: AE, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU,
              CZ, CZ, DE, DE, DK, DK, EE, EE, ES, FI, FI, GB, GD, GE, GH, GM,
              HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS,
              LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD,
              SE, SG, SI, SK, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU,
              ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
          RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK,
              ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG,
              CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
      SE 9802529
                            20000214
                      Α
                                          SE 1998-2529
                                                            19980713
      AU 9949500
                                          AU 1999-49500
                       Α1
                            20000214
                                                            19990706
      EP 1094851
                       Α1
                            20010502
                                          EP 1999-933447 19990706
          R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
              IE, FI
 PRAI SE 1998-2529
                       Α
                            19980713
      WO 1999-SE1231
                       W
                            19990706
      The invention relates to a prepn. for restoring bone in the body of
 AΒ
 humans
      or animals in connection with an existing structure, a bone implant or
      some other prosthetic construction, as well as a method for restoring
      bone. The bone restoring prepn. consists of an easily handleable and
      controllable prepn. (compn.) of resorbable calcium phosphate
      granules and a carrier of a biopolymer or lipid type. The prepn. is
      intended to be applied in the position where the bone needs to be
      replaced, reinforced or built up, esp. in connection with a bone implant
      or some other prosthetic construction where there is a lack of sufficient
     bone vol., or where the quality of the bone is too poor to allow a
      load-carrying function, for example permanent fixing of an implant. A
      phospholipid (Epikuron 200) was mixed with hydroxylapatite and ethanol.
     This sample was then freeze-dried to a const. wt. After freeze-drying,
      the sample had a compn. of phosphatidylcholine 30.1 and hydroxylapatite
      69.9%. The wt. ratio between the calcium phosphate component
     and the lipid and the admixt. of water were detd. by the requirement that
      the prepn. should be easily handleable and moldable.
 RE.CNT 6
 (1) Bioapatite, A; SE 464912 B 1991 CAPLUS
 (2) Deibig, H; US 4192021 A 1980 CAPLUS
 (3) HArle, A; US 5769897 A 1998
 (4) Hans-JOrg, B; US 5338772 A 1994
 (6) Ontario Inc; WO 9745147 A1 1997 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT
L12
     ANSWER 7 OF 32 CAPLUS COPYRIGHT 2001 ACS
                                                 DUPLICATE 4
AN
     2000:141482 CAPLUS
DN
     132:185482
TI
     Malleable paste for filling bone defects
ΙN
     Gertzman, Arthur A.; Sunwoo, Moon Hae
PΑ
     Musculoskeletal Transplant Foundation, USA
SO
     U.S., 7 pp.
     CODEN: USXXAM
DT
     Patent
LA
     English
FAN.CNT 1
     PATENT NO.
                 KIND DATE
                                          APPLICATION NO. DATE
                     ----
                                          -----
                           20000229 US 1998-31750 19980227
ΡI
     US 6030635 A
AΒ
     The invention is directed toward a malleable bone putty and a flowable
gel
     compn. for application to a bone defect site to promote new bone growth
at
     the site which comprises a new bone growth inducing compd. of
     demineralized lyophilized allograft bone powder. The bone powder has a
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particle size ranging from about 100 to about 850 .mu. and is mixed in a

high mol. wt. hydrogel carrier, the hydrogel component of the carrier ranging from 0.3 to 3.0% of the compn. and having a mol. wt. of about at least 10,000 Daltons. The compn. contains about 25% to about 40% bone powder and can be addnl. provided with BMP's and a sodium phosphate buffer. A malleable putty of 2% soln. hyaluronic acid in isotonic saline with 250-420 .mu. cortical allograft bone powder at 30%. Freeze dried cortical allograft bone (502 mg) of particle size ranging 250-420 .mu. was mixed into 1170 mg of a 2% soln. of sodium hyaluronate in isotonic saline. The bone component is added to achieve a bone concn. of 30% (wt./wt.). The soln. was well mixed and allowed to stand for 2-3 h at room temp. to provide a

RE.CNT 20

RE

- (1) Chen; US 5707962 1998 CAPLUS
- (4) Fitenmuller; US 4610692 1986 CAPLUS
- (5) Hayes; US 4619995 1986 CAPLUS
- (7) John; US 4595713 1986 CAPLUS
- (16) Sasaki; Stimulation of Osteoinduction in Bone Wound Healing by High-Molecular Hyaluronic Acid Bond 1995, V16(1) CAPLUS

malleable putty with excellent formability properties.

- ALL CITATIONS AVAILABLE IN THE RE FORMAT
- L12 ANSWER 8 OF 32 CAPLUS COPYRIGHT 2001 ACS
- AN 2000:98312 CAPLUS
- DN 132:146657
- TI Use of creatine compounds for treatment of bone or cartilage cells and tissues
- IN Wallimann, Theo; Gerber, Isabel
- PA Synergen A.-G., Switz.; Ao-Forschungsinstitut Davos
- SO PCT Int. Appl., 70 pp.
 - CODEN: PIXXD2
- DT Patent
- LA English

FAN.CNT 1

PΙ

PATENT NO. KIND DATE APPLICATION NO. DATE

WO 2000006150 A1 20000210

WO 1998-EP4713 19980728

W: CA, JP, US

RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE

OS MARPAT 132:146657

AB The method, compn. and use of the compn. for healing defects in bone or cartilage tissue in animals and humans caused by trauma or surgery is disclosed. The method comprises administration of creatine compds. including analogs or pharmaceutically acceptable salts thereof.

Treatment

in accordance with this method speeds-up time for and improves the process $% \left(1\right) =\left(1\right) +\left(1\right)$

of healing of defects in bone or cartilage tissue in animals and humans caused by trauma or surgery including acceptance and bonding of artificial

implants. The treatment with creatine compds. can be therapeutic for diseased patients, preventive for healthy people as well as geriatric for elderly people. Creatine stimulated the metabolic activity of rat osteoblasts from the second week onwards. Creatine-treated groups also had significantly more mineralization than the control at two weeks.

RE.CNT 3

RE

- (1) Bruce, R; WO 9745533 A 1997 CAPLUS
- (2) Nutricia Nv; EP 0891719 A 1999 CAPLUS
- (3) Somjensomjen, D; STEROIDS: STRUCTURE, FUNCTION, AND REGULATION 1998, V63(5-6), P340
- L12 ANSWER 9 OF 32 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
- AN 2000-532868 [48] WPIDS
- DNN N2000-394155 DNC C2000-158767

```
Osteogenic paste useful for bone repair in mammals, especially for spinal
ΤI
     fusions comprises resorbable carrier, osteogenic factor and mineral
     particles to provide scaffold.
DC
     B04 D22 P34
IN
     MCKAY, W F
     (SDGI-N) SDGI HOLDINGS INC
PA
CYC
     WO 2000045870 A1 20000810 (200048) * EN
PΙ
        RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL
            OA PT SD SE SL SZ TZ UG ZW
         W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES
            FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS
            LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL
            TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
     AU 2000027564 A 20000825 (200059)
     WO 2000045870 A1 WO 2000-US3024 20000204; AU 2000027564 A AU 2000-27564
     20000204
FDT AU 2000027564 A Based on WO 200045870
PRAI US 1999-118614
                     19990204
     2000-532868 [48]
                        WPIDS
AN
     WO 200045870 A UPAB: 20001001
AΒ
     NOVELTY - Osteogenic paste (A) comprises:
          (i) a resorbable paste carrier (C);
          (ii) osteogenic factor (I) and
          (iii) a porous particulate mineral (II).
          At least 20 vol.% of (A), sufficient to provide a scaffold for bone
     regrowth as (C) is resorbed.
          DETAILED DESCRIPTION - An INDEPENDENT CLAIM is included for an
     osteogenic implant material (A') comprising gelatin as (C), formulated to
     be fluid at above mammalian body temperature but to undergo transition to
     the non-fluid state at body temperature, (I), demineralized bone matrix
     (DBM) and (II) of average particle size 0.05-5 mm at least 20 vol.%.
          ACTIVITY - Osteogenic.
          MECHANISM OF ACTION - Osteoblast stimulator; osteoclast
stimulation.
          USE - (A) Is used to induce new bone growth in mammals, particularly
     primates and specifically humans, i.e. for treating bone trauma, disease
     or defects and for forming artificial arthrodeses. Especially it is used
     to create a spinal fusion (interbody, posterolateral or between
transverse
     processes of adjacent vertebrae).
          ADVANTAGE - (A) Has increased osteoinductive potential but, despite
     the rapid resorption of M induced by (I), it retains a reliable scaffold,
     of (II) particles, for long enough (e.g. 6-8 weeks) for formation of new
     bone. (A) is especially effective in bones with only low or moderate
     vascularization. The paste can be formed into preselected shapes before
     implantation, or during surgery, and retains its dimensional stability.
          The following samples (0.05 ml) were implanted into the rectus
     abdominus muscle of rats: (1) demineralized bone matrix (DBM) only; (2)
     Helistat (RTM for absorbable collagen sponge) containing 0.004 mg of
     recombinant human bone morphogenetic protein-2 (I');
     (3) a gelatin/DBM paste, and (4) as (3) but including 0.001 mg (I').
     Periodically implants were analyzed. Incorporation of (I'), in (4),
     resulted in higher, and earlier, alkaline phosphatase activity
(indicating
     infiltration by osteoinductive cells) and better calcification
(indicative
     of bone formation). Higher levels of (I') (0.002 mg) stimulated
resorption
     of the collagen matrix, leading to loss of osteogenic potential.
     Dwg.0/2
L12 ANSWER 10 OF 32 WPIDS COPYRIGHT 2001
                                             DERWENT INFORMATION LTD
     2000-507223 [46]
ΑN
                        WPIDS
DNC C2000-152167
     Composition containing hydrophobically modified hedgehog protein, useful
ΤI
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for inducing repair of e.g. bone and cartilage, formulated with biodegradable protein carrier. DC IN LANG, K; PAPADIMITRIOU, A (HOFF) ROCHE DIAGNOSTICS GMBH PΑ CYC 91 EP 1025861 A1 20000809 (200046)* DE 14p PΙ R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI WO 2000045848 A1 20000810 (200046) EN RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ TZ UG ZW W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW AU 2000024412 A 20000825 (200059) EP 1025861 A1 EP 1999-101643 19990204; WO 2000045848 A1 WO 2000-EP847 ADT 20000203; AU 2000024412 A AU 2000-24412 20000203 FDT AU 2000024412 A Based on WO 200045848 PRAI EP 1999-101643 19990204 2000-507223 [46] AN WPIDS 1025861 A UPAB: 20000921 AΒ NOVELTY - A pharmaceutical composition (A) comprises a hydrophobically modified hedgehog protein (I) and, as carrier, a biodegradable protein (II). DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for: (1) a method for preparing (A); and (2) a method for sustained release of (I) in the human body by administration of (A). ACTIVITY - Osteogenic; chondrogenic; neurological. MECHANISM OF ACTION - (I) promote the activity and/or expression of alkaline phosphatase. USE - (A) are particularly used for repair of bone and cartilage defects but can also be used for repairing neuronal defects and for systemic delivery of (I). ADVANTAGE - (II) reversibly bind to (I) in its active, folded form and releases it, locally in vivo, in its active state, especially over a period of at least 14 hr. (A) do not induce immunogenic or inflammatory reactions. Lipophilic modification of (I) improves interaction with the lipid membrane of eukaryotic cells. Dwg.0/2 L12 ANSWER 11 OF 32 TOXLIT 2000:7320 TOXLIT AN DN CA-132-185482U ΤI Malleable paste for filling bone defects. ΑU Gertzman AA; Sunwoo MH (2000). U.S. PATENT NO. 6030635 02/29/2000 (Musculoskeletal Transplant SO Foundation). CODEN: USXXAM. CY UNITED STATES DT Patent FS LA English OS CA 132:185482 ΕM 200003 AΒ The invention is directed toward a malleable bone putty and a flowable gel compn. for application to a bone defect site to promote new bone growth at the site which comprises a new bone growth inducing compd. of demineralized lyophilized allograft bone powder. The bone powder has a particle size ranging from about 100 to about 850 .mu. and is mixed in a high mol. wt. hydrogel carrier, the hydrogel component of the carrier

ranging from 0.3 to 3.0% of the compn. and having a mol. wt. of about at

least 10,000 Daltons. The compn. contains about 25% to about 40% bone powder and can be addnl. provided with BMP's and a sodium phosphate buffer. A malleable putty of 2% soln. hyaluronic acid in isotonic saline with 250-420 .mu. cortical allograft bone powder at 30%. Freeze dried cortical allograft bone (502 mg) of particle size ranging 250-420 .mu. was mixed into 1170 mg of a 2% soln. of sodium hyaluronate in isotonic saline. The bone component is added to achieve a bone concn. of 30% (wt./wt.). The soln. was well mixed and allowed to stand for 2-3 h at room temp. to provide a malleable putty

with
 excellent formability properties.

- L12 ANSWER 12 OF 32 CAPLUS COPYRIGHT 2001 ACS
- AN 2000:672409 CAPLUS
- DN 134:168254
- TI Injectable hyaluronic acid/tricalcium phosphate composites for the delivery of rhBMP-2
- AU Kim, H. D.; Li, R.; Augusta, D. A. D'; Bouxsein, M.; Blake, C.; Luppen, C.; Seeherman, H.; Wozney, J. M.
- CS Genetics Institute, Inc., Andover, MA, 01810, USA
- SO Proc. Int. Symp. Controlled Release Bioact. Mater. (2000), 27th, 978-979 CODEN: PCRMEY; ISSN: 1022-0178
- PB Controlled Release Society, Inc.
- DT Journal
- LA English
- AB Addn. of tricalcium phosphate (TCP) to partial or full esters of hyaluronic acid injectable carriers enhanced retention of rhBMP-2 in vitro. Retention of rhBMP-2 in vivo at the local fracture site was enhanced when delivered in hyaluronic acid/TCP blends compared to buffer delivery. Partial esters of hyaluronic acid and their blends with TCP enhanced fracture repair compared to control limbs in the rabbit model.
- L12 ANSWER 13 OF 32 MEDLINE
- AN 2000106511 MEDLINE
- DN 20106511 PubMed ID: 10643717
- TI Osteogenic protein 1 stimulates cells-associated matrix assembly by normal human articular chondrocytes: up-regulation of hyaluronan synthase, CD44, and aggrecan.
- AU Nishida Y; Knudson C B; Eger W; Kuettner K E; Knudson W
- CS Rush Medical College, Rush-Presbyterian-St. Luke's Medical Center, Chicago, Illinois 60612, USA.
- NC P50-AR-39239 (NIAMS) R01-AR-39507 (NIAMS) R01-AR-43384 (NIAMS)
- SO ARTHRITIS AND RHEUMATISM, (2000 Jan) 43 (1) 206-14. Journal code: 90M; 0370605. ISSN: 0004-3591.
- CY United States
- DT Journal; Article; (JOURNAL ARTICLE)
- LA English
- FS Abridged Index Medicus Journals; Priority Journals
- EM 200002
- ED Entered STN: 20000209 Last Updated on STN: 20000209 Entered Medline: 20000203
- AB OBJECTIVE: To determine the effects of **osteogenic**protein 1 (OP-1) on hyaluronan (HA),

 CD44, and aggrecan biosynthesis as well as the contribution of these
 molecules in promoting matrix assembly by human articular chondrocytes.

 METHODS: Normal human chondrocytes were cultured with or without

 OP-1 treatment. Changes in the relative expression of

messenger RNA (mRNA) for HA synthases 2 and 3 (HAS-2 and HAS-3), CD44, and

aggrecan were determined by competitive quantitative reverse transcriptase-polymerase chain reaction. Accumulation of HA was characterized by indirect staining, CD44 by flow cytometry, and aggrecan

biosynthesis by 35SO4 incorporation. RESULTS: OP-1 stimulated the expression of HAS-2, CD44, and aggrecan mRNA in a time-dependent manner, resulting in increased expression of HA, CD44, and aggrecan. Prominent increases in HA-rich cell-associated matrices were also observed. CONCLUSION: OP-1 stimulates not only the synthesis of matrix macromolecules such as aggrecan, but also the synthesis of other molecules required for matrix retention, namely, HA and CD44. L12 ANSWER 14 OF 32 BIOSIS COPYRIGHT 2001 BIOSIS 2000:288137 BIOSIS ΑN PREV200000288137 DN The importance of drug delivery systems in tissue engineering. ΤI Tabata, Yasuhiko ΑU Pharmaceutical Science & Technology Today, (March, 2000) Vol. 3, No. 3, SO pp. 80-89. print.. ISSN: 1461-5347. DTArticle English LASL English Tissue engineering is designed to regenerate natural tissues or to create ΑB biological substitutes for defective or lost tissues and organs through the use of cells. In addition to cells and their scaffolds, growth factors are required to promote tissue regeneration. Indeed, growth factor-induced vascularization is effective in supplying the oxygen and nutrients necessary for the survival of transplanted cells in organ substitution. However, growth factors have poor in vivo stability and so the biological effects are often unpredictable unless the delivery system is contrived. This review provides several examples to emphasize the importance of drug delivery systems in tissue engineering. L12 ANSWER 15 OF 32 CAPLUS COPYRIGHT 2001 ACS 1999:795994 CAPLUS AN 132:31744 DN Gene probes used for genetic profiling in healthcare screening and ΤI planning Roberts, Gareth Wyn IN PΑ Genostic Pharma Ltd., UK SO PCT Int. Appl., 745 pp. CODEN: PIXXD2 DT Patent LA English FAN.CNT 2 PATENT NO. KIND DATE APPLICATION NO. DATE _____ ---------WO 9964627 A2 19991216 WO 1999-GB1780 19990604 ΡI W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG PRAI GB 1998-12099 Α 19980606 GB 1998-13291 19980620 Α GB 1998-13611 Α 19980624 GB 1998-13835 Α 19980627 GB 1998-14110 A 19980701 GB 1998-14580 A 19980707 GB 1998-15438 A 19980716

A 19980718

GB 1998-15574

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GB 1998-16085 A
GB 1998-16086
                           19980718
                           19980724
                    A 19980724
    GB 1998-16921
                          19980805
                    Α
    GB 1998-17097
                          19980807
                    Α
    GB 1998-17200
                          19980808
                    Α
    GB 1998-17632
                     A
                          19980814
    GB 1998-17943
                     Α
                          19980819
    There is considerable evidence that significant factor underlying the
    individual variability in response to disease, therapy and prognosis lies
    in a person's genetic make-up. There have been numerous examples
    that polymorphisms within a given gene can alter the functionality of the
    protein encoded by that gene thus leading to a variable physiol.
    In order to bring about the integration of genomics into medical practice
    and enable design and building of a technol. platform which will enable
    the everyday practice of mol. medicine a way must be invented for the DNA
    sequence data to be aligned with the identification of genes central to
    the induction, development, progression and outcome of disease or
     states of interest. According to the invention, the no. of genes and
    their configurations (mutations and polymorphisms) needed to be
    in order to provide crit. clin. information concerning individual
    prognosis is considerably less than the 100,000 thought to comprise the
    human genome. The identification of the identity of the core group of
    genes enables the invention of a design for genetic profiling
technologies
    which comprises of the identification of the core group of genes and
    sequence variants required to provide a broad base of clin. prognostic
    information - "genostics". The "Genostic.RTM." profiling of patients and
    persons will radically enhance the ability of clinicians, healthcare
    professionals and other parties to plan and manage healthcare provision
    and the targeting of appropriate healthcare resources to those deemed
most
    in need. The use of this invention could also lead to a host of new
    applications for such profiling technologies, such as identification of
    persons with particular work or environment related risk, selection of
    applicants for employment, training or specific opportunities or for the
    enhancing of the planning and organization of health services, education
    services and social services.
L12 ANSWER 16 OF 32 CAPLUS COPYRIGHT 2001 ACS
AN
    1999:795993 CAPLUS
DN
    132:31743
ΤI
    Gene probes used for genetic profiling in healthcare screening and
    planning
ΙN
    Roberts, Gareth Wyn
    Genostic Pharma Limited, UK
PΑ
SO
    PCT Int. Appl., 149 pp.
    CODEN: PIXXD2
DT
    Patent
LA
    English
FAN.CNT 2
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KIND DATE
                                      APPLICATION NO. DATE
    PATENT NO.
                   ____
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                                       -----
    WO 9964626 A2 19991216
                                      WO 1999-GB1779 19990604
PΤ
        W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ,
           DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS,
            JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK,
           MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ,
           TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ,
           MD, RU, TJ, TM
        RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK,
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ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG,
             CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
     AU 9941586
                        A1
                             19991230
                                             AU 1999-41586
                                                               19990604
                                             AU 1999-41587
                                                               19990604
     AU 9941587
                        A1
                             19991230
                                             GB 1999-12914
                             20000119
                                                               19990604
     GB 2339200
                        A1
                             20010321
                                             EP 1999-925207
                                                               19990604
     EP 1084273
                       Α1
         R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, FI
PRAI GB 1998-12098
                             19980606
     GB 1998-28289
                       Α
                             19981223
     GB 1998-16086
                       Α
                             19980724
     GB 1998-16921
                       Α
                             19980805
     GB 1998-17097
                       Α
                             19980807
     GB 1998-17200
                       Α
                             19980808
     GB 1998-17632
                        Α
                             19980814
     GB 1998-17943
                        Α
                             19980819
     WO 1999-GB1779
                       W
                             19990604
     There is considerable evidence that significant factor underlying the
AΒ
     individual variability in response to disease, therapy and prognosis lies
     in a person's genetic make-up. There have been numerous examples
relating
     that polymorphisms within a given gene can alter the functionality of the
     protein encoded by that gene thus leading to a variable physiol.
response.
     In order to bring about the integration of genomics into medical practice
     and enable design and building of a technol. platform which will enable
     the everyday practice of mol. medicine a way must be invented for the DNA
     sequence data to be aligned with the identification of genes central to
     the induction, development, progression and outcome of disease or
physiol.
     states of interest. According to the invention, the no. of genes and
     their configurations (mutations and polymorphisms) needed to be
identified
     in order to provide crit. clin. information concerning individual
     prognosis is considerably less than the 100,000 thought to comprise the
     human genome. The identification of the identity of the core group of
     genes enables the invention of a design for genetic profiling
     technologies.
     ANSWER 17 OF 32 CAPLUS COPYRIGHT 2001 ACS
L12
     1999:64926 CAPLUS
AN
DN
     130:134991
     Xenopus WA545 protein compositions and their function in induction of
TI
     mesodermal or related tissue formation
     Lavallie, Edward R.; Racie, Lisa A.; Sive, Hazel; Sun, Benjamin
ΙN
     Genetics Institute, Inc., USA; The Whitehead Institute for Biomedical
PΑ
     Research
     PCT Int. Appl., 74 pp.
SO
     CODEN: PIXXD2
DT
     Patent
LΑ
     English
FAN.CNT 1
                                            APPLICATION NO.
     PATENT NO.
                       KIND
                             DATE
                                                               DATE
                       ____
                             _____
                                             -----
     WO 9902678
                      A1
                             19990121
                                           WO 1998-US8334
                                                               19980424
PΙ
         W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE,
             DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG,
             KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT,
         UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES,
             FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG
                       Al
     AU 9871597
                             19990208
                                             AU 1998-71597
                                                               19980424
                                           EP 1998-918722
     EP 998558
                        Α1
                             20000510
                                                               19980424
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R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,

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IE, FI
                      19970710
PRAI US 1997-890918
                           19980424
    WO 1998-US8334
    Purified Xenopus WA545 proteins and processes for producing them are
AB
    disclosed. A cDNA clone encoding the full-length WA545 proteins are also
    disclosed. WA545 is expressed from late blastula throughout the mesoderm
    and endoderm. It is later expressed in posterior mesoderm. Is is able
to
    efficiently induce posterior and lateral mesoderm, including muscle.
    Thus, WA545 may be involved in formation of posterior regions and may be
    useful for ectopic activation of muscle and spinal cord development. The
    proteins, members of the TGF-.beta. superfamily of growth factors, may be
    used to induce, enhance and/or inhibit the information, growth,
    proliferation, differentiation, maintenance of mesodermal tissue,
     including neural and muscle tissue. The proteins may also be useful for
     treatment of bone and cartilage and/or other connective tissue defects
and
     in wound healing and related tissue repair.
RE.CNT 4
RE
(1) Creative Biomolecules Inc; WO 9406449 A 1994 CAPLUS
(2) Dale, L; Embo Journal 1993, V12(12), P4471 CAPLUS
(3) Jacobs, K; US 5536637 A 1996 CAPLUS
(4) Weeks, D; Cell 1987, V51, P861 CAPLUS
L12 ANSWER 18 OF 32 CAPLUS COPYRIGHT 2001 ACS
    1999:772568 CAPLUS
AN
DN
     132:15641
     Ophthalmologic eye lotions containing polymers with side-chains of
TI
     phosphorylcholine analogs
     Miyazaki, Takeshi; Nakata, Shinji; Ando, Ryota; Nakabayashi, Nobuo;
ΙN
     Ishihara, Kazuhiko
     Nippon Oil and Fats Co., Ltd., Japan
PA
     Jpn. Kokai Tokkyo Koho, 11 pp.
SO
     CODEN: JKXXAF
DΤ
     Patent
     Japanese
LA
FAN.CNT 1
                                         APPLICATION NO. DATE
     PATENT NO.
                 KIND DATE
                     ____
                           _____
     JP 11335301 A2 19991207 JP 1998-139798 19980521
     The side chains are -OP(:0)(O-)O(CH2)mN-R1R2R3 where R1, R2, and
     R3 = H C1-4  alkyl; m = 2-4. Pharmaceutical active agents with the
polymer
     in eye lotions applied to the eye remain on the surface of the cornea for
     a long period.
L12 ANSWER 19 OF 32 MEDLINE
ΑN
     1999069840
                   MEDLINE
DN
     99069840 PubMed ID: 9852738
TΙ
     Osteotransductive bone cements.
     Driessens F C; Planell J A; Boltong M G; Khairoun I; Ginebra M P
ΑU
     Department of Materials Science and Metallurgy, Universitat Politecnica
CS
de
     Catalunya, Barcelona, Spain.
     PROCEEDINGS OF THE INSTITUTION OF MECHANICAL ENGINEERS. PART H, JOURNAL
SO
OF
     ENGINEERING IN MEDICINE, (1998) 212 (6) 427-35.
     Journal code: ABJ; 8908934. ISSN: 0954-4119.
     ENGLAND: United Kingdom
CY
     Journal; Article; (JOURNAL ARTICLE)
DT
LA
     English
     Priority Journals
FS
EM
     199901
     Entered STN: 19990115
ED
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Last Updated on STN: 19990115

Entered Medline: 19990104

Calcium phosphate bone cements (CPBCs) are osteotransductive, AΒ i.e. after implantation in bone they are transformed into new bone tissue.

Furthermore, due to the fact that they are mouldable, their osteointegration is immediate. Their chemistry has been established previously. Some CPBCs contain amorphous calcium phosphate (ACP) and set by a sol-gel transition. The others are crystalline and can give as the reaction product dicalcium phosphate dihydrate (DCPD), calcium-deficient hydroxyapatite (CDHA), carbonated apatite (CA) or hydroxyapatite (HA). Mixed-type gypsum-DCPD cements are also described. In vivo rates of osteotransduction vary as follows: gypsum-DCPD > DCPD > CDHA approximately CA > HA. The osteotransduction of CDHA-type cements may be increased by adding dicalcium phosphate anhydrous (DCP) and/or CaCO3 to the cement powder. CPBCs can be used for healing of bone defects, bone augmentation and bone reconstruction. Incorporation of drugs like antibiotics and bone morphogenetic protein is envisaged. Load-bearing applications are allowed for CHDA-type, CA-type and HA-type CPBCs as they have a higher compressive strength than human trabecular bone (10 MPa).

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L12 ANSWER 20 OF 32 CAPLUS COPYRIGHT 2001 ACS
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1999:313175 CAPLUS AN

130:316664 DN

Biologically active material and process for its preparation TΙ

Vanis, Matej; Bakos, Dusan; Vanis, Peter; Makai, Frantisek; Macho, ΙN Vendelin

Chemickotechnologicka Fakulta Stu, Slovakia PA

Czech Rep., 7 pp. CODEN: CZXXED

DTPatent

LA Czech

FAN.CNT 1

DATE APPLICATION NO. DATE PATENT NO. KIND DATE _____ ____ CZ 283073 B6 19971217 CZ 1992-3295 19921103

PΙ The prepn. of bioactive ossifying material suitable for bone implants in AB reconstructive surgery is described. The prepn. contains Ca phosphate and/or Ca fluorophosphate particles 0.1-0.6 mm mixed with atelocollagen I in mass ratios of 1.5:1 to 50:1. Atelocollagen I

can

be prepd. by enzymic hydrolysis of bovine tendons. The prepn. can further

contain 0.01-5.0% hyaluronic acid or its salts (related to material dry matter), 1-20% bone morphogenetic proteins extd. from bovine bones, and adjuvants components (blood, blood plasma, artificial body fluids). During prepn. the components are homogenized together. The formed ppt. is formed into desired implant shape or dried and powd. The material is sterilized by .gamma.-radiation. Before use the powd. material is reconstituted with physiol. fluids and formed into desired shapes. The biol. compatibility was tested in dogs with exptl. tibial bone injury.

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L12 ANSWER 21 OF 32 TOXLIT
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1997:166800 TOXLIT AN

DN CA-130-316664P

Biologically active material and process for its preparation. ΤI

Vanis M; Bakos D; Vanis P; Makai F; Macho V ΑU

(1997). Czech Rep. PATENT NO. 283073 12/17/1997 (Chemickotechnologicka SO Fakulta Stu). CODEN: CZXXED.

CY SLOVAKIA

DTPatent

FS CA

LA Czech

OS CA 130:316664 EM 199905

The prepn. of bioactive ossifying material suitable for bone implants in reconstructive surgery is described. The prepn. contains Ca phosphate and/or Ca fluorophosphate particles 0.1-0.6 mm mixed with atelocollagen I in mass ratios of 1.5:1 to 50:1. Atelocollagen I can be prepd. by enzymic hydrolysis of bovine tendons. The prepn. can further contain 0.01-5.0% hyaluronic acid or its salts (related to material dry matter), 1-20% bone morphogenetic proteins extd. from bovine bones, and adjuvants components (blood, blood plasma, artificial body fluids). During prepn. the components are homogenized together. The formed ppt. is formed into desired implant shape or dried and powd. The material is sterilized by .gamma.-radiation. Before use the powd. material is reconstituted with physiol. fluids and formed into desired shapes. The biol. compatibility was tested in dogs with exptl. tibial bone injury.

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L12 ANSWER 22 OF 32 CAPLUS COPYRIGHT 2001 ACS
    1997:107401 CAPLUS
AN
    126:122511
DN
    Biocompatible hydroxyapatite formulations for medical and dental use
TΙ
     Constantino, Peter D.; Friedman, Craig D.; Sen, Arup
ΙN
PΑ
     Osteogenics Inc., USA
     PCT Int. Appl., 77 pp.
SO
    CODEN: PIXXD2
\mathsf{DT}
     Patent
LA
    English
FAN.CNT 1
                                        APPLICATION NO. DATE
                 KIND DATE
     PATENT NO.
                                         _____
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                     ____
                           19961212
                                       WO 1996-US8652 19960603
     WO 9639202 A1
PΙ
        W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE,
            ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS,
            LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD,
        RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR,
            IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN
                                         CA 1996-2223596 19960603
                           19961212
     CA 2223596
                      AA
                                         AU 1996-61496
                      A1
                           19961224
                                                          19960603
     AU 9661496
     AU 723740
                      В2
                           20000907
                                         EP 1996-919055
     EP 830149
                      A1
                           19980325
                                                          19960603
           AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
            IE, FI
                                          BR 1996-8344
                                                          19960603
     BR 9608344
                           19990105
                      Α
                                          JP 1996-501179
                                                          19960603
                      Т2
                           19990615
     JP 11506659
                    Α
                           19950606
PRAI US 1995-468084
                    A
     US 1995-469909
                           19950606
                    A
                           19950606
     US 1995-471216
                     W
     WO 1996-US8652
                           19960603
     A biocompatible hydroxyapatite formulation is pptd. from a mixt. of a
AΒ
liq.
     phase, a bioactive or biocompatible additive which may be any of a no. of
     bioreactive or other substances, and a base combination of calcium
     phosphate salts. The liq. phase and the additive may be combined
     to produce an augmented liq. phase, which is then mixed with the base
salt
     combination. The additive is chosen to achieve a desired effect during
     administration of the formulation to a plant or animal. The additive in
     released into the surrounding physiol. milieu and the hydroxyapatite
     component is resorbed (no data).
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L12 ANSWER 23 OF 32 CAPLUS COPYRIGHT 2001 ACS

Studies of the integration between bone morphogenetic

protein treated titanium/bioceramic composite and host bone after

1996:386327 CAPLUS

125:82695

implantation

AN DN

TI

Guo, Qingke; Tang, Wenjie; Xiao, Guangyu; Wang, Hong; Yan, Ying; Wu, AU Bende; Liao, Jichang; Pang, Wei Tangdu Hospital, Fourth Military Medical University, Xian, 710038, Peop. CS Rep. China Disi Junyi Daxue Xuebao (1996), 17(2), 138-140 SO CODEN: DJDXEG; ISSN: 1000-2790 DT Journal Chinese LA The porous, bioactive titanium/glass-ceramic composite was made from Tc4, AΒ HA and BGC, which were sintered at high temp. The composite material treated with bone morphogenetic protein (BMP) was implanted in jaw and femur of adult dogs for 1.apprx.12 wk. bone-implant interfaces were studied and the content of new bone formation was measured. The results showed that the integration of the composite material and host bone was formed, and the interface consists of three phases (titanium oxide, HA crystal phase, glass ceramic phase) in the interface. A layer of calcium phosphate and bioceramic deposition were formed. The combination of proteoglycan mucoitin with host bone and the inducement of calcium phosphate deposition might play an important role in the osteointegration between implant and bone. The process of osteogenesis was enhanced by treatment of implant material with BMP. L12 ANSWER 24 OF 32 CAPLUS COPYRIGHT 2001 ACS 1994:253359 CAPLUS AN DN 120:253359 Biocompatible polymer conjugates of natural polymers TIRhee, Woonza; Wallace, Donald G.; Michaels, Alan S.; Burns, Ramon A., IN Jr.; Fries, Louis; Delustro, Frank; Bentz, Hanne; Mccullough, Kimberly; Damani, Ramesh; Berg, Richard A. PACollagen Corp., USA PCT Int. Appl., 103 pp. SO CODEN: PIXXD2 DT Patent LA English FAN.CNT 18 PATENT NO. KIND DATE APPLICATION NO. DATE _____ _____ _____ ____ WO 1993-US6292 19930701 WO 9401483 A1 19940120 PΙ W: AU, JP RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE US 1992-907518 US 5324775 A 19940628 19920702 US 1992-922541 19920730 US 5328955 Α 19940712 US 1992-985680 Α 19921202 US 5292802 19940308 Α US 1992-984197 US 5308889 19940503 19921202 A1 AU 1993-46620 AU 9346620 19940131 19930701 AU 677789 B2 EP 648239 A1 19970508 19950419 EP 1993-916926 19930701 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE JP 1993-503427 19930701 19960305 JP 08502082 Т2 19920702 PRAI US 1992-907518 A А US 1992-922541 19920730 Α US 1992-984197 19921202 A 19921202 US 1992-984933 US 1992-985680 A 19921202 A 19930302 B2 19881121 Α US 1993-25032 US 1988-274071 A2 19891114 A 19930701 US 1989-433441 WO 1993-US6292

Non-immunogenic conjugates are formed by covalently binding a biol.

inactive, natural polymer or deriv. thereof to synthetic hydrophilic polymers, e.g. PEG, via specific types of chem. bonds. The biocompatible

AΒ

conjugates can be used for soft tissue augmentation and for coating or forming various articles. The compns. may include other components such as liq., pharmaceutically acceptable carriers to form injectable formulations, and/or biol. active proteins such as growth factors or cytokines. A soln. of transforming growth factor .beta.1 (TGF-.beta.1) was added to a soln. of difunctionally activated PEG and the mixt. was allowed to react for 2 min at 17.degree.. To this soln. was added a fibrillar atelopeptide collagen soln. and the resulting mixt. allowed to incubate overnight at ambient temp. to form pellets comprising collagen-PEG-TGF-.beta.1 conjugate. After washing the pellets 6 times with **phosphate** buffer .apprx.50% of TGF-.beta.1 was retained in the compn.

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L12 ANSWER 25 OF 32 BIOSIS COPYRIGHT 2001 BIOSIS
    1994:324820 BIOSIS
AN
DN
    PREV199497337820
    Histological features of connective tissues.
TΙ
    Byers, Paul D.
ΑU
    18 Wimpole St., London W1M 7AD UK
CS
    Salisbury, J. R. [Editor]; Woods, C. G. [Editor]; Byers, P. D. [Editor].
SO
     (1994) pp. 476-508. Diseases of bones and joints: Cell biology,
    mechanisms, pathology.
     Publisher: Chapman and Hall Ltd. 2-6 Boundary Row, London SE1 8HN,
    England.
     ISBN: 0-412-48010-7.
DT
     Book
    English
LA
    ANSWER 26 OF 32 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
     94272250 EMBASE
AN
     1994272250
DN
     Binding and growth-inhibitory effect of heparin and oligo-heparin (2 kDa)
TI
     in Balb/c 3T3 cells: Lack of effect on PDGF- or serum-induced inositol
     lipid turnover.
     Cavari S.; Fiorelli G.; Vannucchi S.
ΑU
     Istituto di Patologia Generale, University of Firenze, Viale Morgagni
CS
     50,50134 Firenze, Italy
     British Journal of Pharmacology, (1994) 113/1 (254-260).
SO
     ISSN: 0007-1188 CODEN: BJPCBM
CY
     United Kingdom
DT
     Journal; Article
FS
     023
             Nuclear Medicine
             Clinical Biochemistry
     029
     030
             Pharmacology
             Drug Literature Index
     037
     English
LA
SL
     English
     The ability of heparins (bovine heparin sm 1026, Av. mol. wt. 36.9 kDa
AB
and
     bovine heparin EP 756, Av. mol. wt. 12.9 kDa) and heparin fractions of
     different molecular weights (low molecular weight heparin, LMW 2123/
     OP, Av. mol. wt. 4.5 kDa and oligo-heparin, Av. mol. wt. 2 kDa) to
     inhibit the proliferation and signalling of Balb/c 3T3 fibroblasts was
     investigated. Heparin and heparin fractions of 4.5 and 2 kDa
significantly
     inhibited DNA synthesis as monitored by [3H]-thymidine incorporation.
     3H-labelled heparin fractions of 4.5 and 2 kDa were prepared by
     gel-chromatography fractionation on Sephadex G-75 of an 3H-labelled
     commercial heparin after treatment with heparinase. The binding of
     unfractionated and oligo-heparin of 2 kDa to Balb/c 3T3 fibroblasts was
     studied; we determined the specificity of heparin and oligo-heparin
     binding to the cells by means of displacement of bound 3H-labelled
     compound in response to increasing concentrations of unlabelled
compounds.
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Scatchard analysis of binding data obtained using [3H]-heparin as ligand revealed the presence of a single class of high affinity binding sites

(K(d) = 28 nM) for heparin. Scatchard analysis of binding data obtained using [3H]-oligo-heparin as ligand revealed the presence of a single class

of low affinity binding sites (K(d) = 3.2 .mu.M) for oligo-heparin. In addition heparin displaced [3H]-oligo-heparin at a concentration of approximately 100 fold of the K(d) determined in displacement studies. Furthermore, oligo-heparin significantly displaced [3H]-heparin at a concentration of approximately 10 fold of the K(d) determined by displacement studies. Both heparin and oligo-heparin exert their inhibitory effects on Balb/c 3T3 DNA synthesis stimulated by PDGF or serum. However these molecules did not affect the inositol lipid turnover triggered by PDGF at a concentration which did not produce maximal response. The increase of inositol **phosphate** metabolism produced by 20% serum was also unaffected by heparin. This concentration of serum elicited a response comparable to that induced by a submaximal concentration of PDGF.

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L12 ANSWER 27 OF 32 CAPLUS COPYRIGHT 2001 ACS
    1993:588652 CAPLUS
ΑN
    119:188652
DN
    Porous non-toxic implant
TI
     Johansson, Thomas
ΙN
    Lucocer Aktiebolag, Swed.
PΑ
    PCT Int. Appl., 13 pp.
SO
    CODEN: PIXXD2
DT
     Patent
    English
LA
FAN.CNT 1
                                        APPLICATION NO. DATE
     PATENT NO. KIND DATE
                          _____
                    ____
    WO 9313815 A1
                           19930722
                                        WO 1992-SE784
PΙ
        W: AT, AU, BB, BG, BR, CA, CH, CS, DE, DK, ES, FI, GB, HU, JP, KP,
            KR, LK, LU, MG, MN, MW, NL, NO, PL, RO, RU, SD, SE, US
        RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, SE, BF,
            BJ, CF, CG, CI, CM, GA, GN, ML, MR, SN, TD, TG
                                         SE 1992-72
                                                          19920113
                           19930714
     SE 9200072
                     A
     SE 469653
                      В
                           19930816
                      С
                           19931209
     SE 469653
                                         AU 1993-32699
                     A1
                           19930803
                                                          19921113
     AU 9332699
                                         EP 1993-901443
    EP 623031 A1
EP 623031 B1
                           19941109
                                                          19921113
                           20000202
        R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, NL
                                                          19921113
                                        JP 1992-512370
     JP 07506732 T2
                           19950727
                                         AT 1993-901443
                                                          19921113
                      Ε
                           20000215
     AT 189401
PRAI SE 1992-72
                           19920113
     WO 1992-SE784
                           19921113
     An implant comprises a porous non-toxic material, e.g. Ti, having a total
AB
     open porosity of 5-80% by vol. The communicating micropores, having a
     size of .gtoreq.10.mu.m, make up .ltoreq.10% of the total pore vol. in at
     least 1 portion of the implant, and .gtoreq.5% of at least 1 section of
     the surface of the implant is covered evenly by distributed pores having
a
     pore size .gtoreq.50.mu.m. The pores contain a bone-promoting agent,
e.g.
     IGF, in a carrier.
     ANSWER 28 OF 32 CAPLUS COPYRIGHT 2001 ACS
L12
     1994:86532 CAPLUS
ΑN
     120:86532
DN
ΤI
     Absorbable bone sealant
     Light, Nicholas D.; Gorham, Steven D.; French, Derek A.
ΙN
     Johnson and Johnson Medical, Inc., USA
PA
SO
     Eur. Pat. Appl., 8 pp.
     CODEN: EPXXDW
```

DT

LA

Patent

English

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FAN.CNT 1
     PATENT NO. KIND DATE
                                           APPLICATION NO. DATE
     ______
                                           _____
                 A1 19931201
B1 19990811
                                           EP 1993-304178 19930528
    EP 572272
PΤ
     EP 572272
        R: AT, BE, CH, FR, GB, IT, LI, LU, NL, PT, SE
    AU 9338786 A1 19931202
AU 669519 B2 19960613
                                           AU 1993-38786
                                                            19930524
    AU 669519 B2 19960613
CA 2097268 AA 19931130 CA 1993-2097268 19930528
BR 9302089 A 19931207 BR 1993-2089 19930528
AT 183103 E 19990815 AT 1993-304178 19930528
PRAI GB 1992-11432
                           19920529
   An absorbable bone sealant compns. comprise a fibrous protein, e.g
     collagen 10-70; a tackifying agent, e.g. dextran 1-20; a
     mucopolysaccharide, e.g. hyaluronic acid 0.001-20; and a
     physiol. acceptable electrolyte soln., e.g. phosphate-buffered
     physiol. saline 10-80%. The compns. are malleable, absorbable,
     biocompatible and exhibit excellent storage properties at 30.degree.C.
     Glycerol 30, and dextran-70 8 g were dissolved in 27mL of water, then
17.5
     g of solubilized collagen and 17.5 g of fibrin powder was dispersed in
the
     soln. by mixing to obtain an absorbable sealant compn. which was
     sterilized by .gamma.-irradn.
L12 ANSWER 29 OF 32 CAPLUS COPYRIGHT 2001 ACS
     1990:637890 CAPLUS
AN
     113:237890
DN
     Manufacture of collagen membranes as dental prosthetics
ΤI
     Kuboki, Yoshinori; Kato, Hiromu
IN
     Sangi Co., Ltd., Japan
Jpn. Kokai Tokkyo Koho, 5 pp.
PΑ
SO
     CODEN: JKXXAF
DT
     Patent
LA
     Japanese
FAN.CNT 1
     PATENT NO. KIND DATE APPLICATION NO. DATE
     JP 02156954 A2 19900615
JP 06069486 B4 19940907
                                           JP 1988-309845 19881209
PΙ
     A collagen membrane as a prosthetic material that helps generate dental
AΒ
     tissues is prepd. by treating collagen fibers with a crosslinking agent
or
     NaBO4 and mixing the fibers with bone-forming proteins
     , hyaluronic acid, chondroitinsulfuric acid, fibronectin,
     osteonectin, etc. Thus, a collagen membrane was obtained by sterilizing
     bovine skin collagen, making it into a flat gel in a phosphate
     buffer, treating it with NaBH4, eliminating water, further dehydrating
     with EtOH, and drying under reduced pressure.
L12 ANSWER 30 OF 32 TOXLIT
     1991:3843 TOXLIT
AN
     CA-113-237890E
DN
     Manufacture of collagen membranes as dental prosthetics.
TI
     Kuboki Y; Kato H
ΑU
     (1990). Jpn. Kokai Tokkyo Koho PATENT NO. 90156954 06/15/90 (Sangi Co.,
SO
     Ltd.).
CY
     Japan
DT
     Patent
FS
     CA
LA
     Japanese
     CA 113:237890
OS
EΜ
     199101
     A collagen membrane as a prosthetic material that helps generate dental
AB
     tissues is prepd. by treating collagen fibers with a crosslinking agent
```

or

NaBO4 and mixing the fibers with bone-forming proteins, hyaluronic acid, chondroitinsulfuric acid, fibronectin, osteonectin, etc. Thus, a collagen membrane was obtained by sterilizing bovine skin collagen, making it into a flat gel in a phosphate buffer, treating it with NaBH4, eliminating water, further dehydrating with EtOH, and drying under reduced pressure.

L12 ANSWER 31 OF 32 MEDLINE

DUPLICATE 5

AN 90367368 MEDLINE

DN 90367368 PubMed ID: 2118436

- Bone morphogenetic protein-mediated interaction of periosteum and diaphysis. Citric acid and other factors influencing the generation of parosteal bone.
- AU Kubler N; Urist M R
- CS Universitatsklinik u. Polikliniken f. Zahn-, Mund- u. Kieferkrankheiten, Wurzburg, Federal Republic of Germany.
- NC DEO2103 (NIDCR)
- SO CLINICAL ORTHOPAEDICS AND RELATED RESEARCH, (1990 Sep) (258) 279-94. Journal code: DFY; 0075674. ISSN: 0009-921X.
- CY United States
- DT Journal; Article; (JOURNAL ARTICLE)
- LA English
- FS Abridged Index Medicus Journals; Priority Journals
- EM 199010
- ED Entered STN: 19901109

Last Updated on STN: 19970203

Entered Medline: 19901005

AB In rabbits, after long-bone growth is complete and the cambium layer regresses, mesenchymal-type cells with embryonic potential (competence) for bone development persist in the adventitial layer of periosteum.

These

cells are not determined osteoprogenitor cells (stem cells) because bone tissue differentiation does not occur when adult periosteum is transplanted into a heterotopic site. In this respect, adventitial cells differ from bone marrow stroma cells. In a parosteal orthotopic site in the space between the adult periosteum and diaphysis, implants of bone morphogenetic protein (BMP) and associated noncollagenous proteins (BMP/NCP) induce adventitia and adjacent muscle connective-tissue-derived cells to switch from a fibrogenetic to a chondroosteoprogenetic pattern of bone development. The quantity of induced bone is proportional to the dose of BMP/NCP in the range from 10 to 50 mg; immature rabbits produced larger deposits than mature rabbits in response to BMP/NCP. Preoperative local intramuscular injections of citric, edetic, or hyaluronic acids in specified concentrations markedly enhanced subperiosteal BMP /NCP-induced bone formation. The quantity of bovine or human BMP /NCP-induced bone formation in rabbits is also increased by very low-dose immunosuppression but not by bone mineral, tricalcium phosphate ceramic, inorganic calcium salts, or various space-occupying, unspecific chemical irritants. Although composities of BMP/NCP and allogeneic rabbit tendon collagen increased the quantity of bone in a parosteal site, in a heterotopic site the composite failed to induce bone formation. In a parosteal site, the conditions permitting BMP /NCP-induced bone formation develop, and the end product of the morphogenetic response is a duplicate diaphysis. How BMP reactivates the morphogenetic process in postfetal mesenchymal-type adventitial cells persisting in adult periosteum (including adjacent muscle attachments) is not known.

- L12 ANSWER 32 OF 32 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
- AN 78214346 EMBASE
- DN 1978214346
- TI Effect of cholecystokinin variant (CCK39) on dispersed acinar cells from guinea pig pancreas.
- AU Sjodin L.; Gardner J.D.
- CS Sect. Gastroenterol., Dig. Dis. Branch, Nat. Inst. Arthr. Metab. Dig.

Dis., NIH, Bethesda, Md. 20014, United States

- SO Gastroenterology, (1977) 73/5 (1015-1018).
- CODEN: GASTAB
 CY United States
- DT Journal
- FS 037 Drug Literature Index
 - 048 Gastroenterology
 - 003 Endocrinology
- LA English
- AB In dispersed acinar cells from guinea pig pancreas, cholecystokinin variants (CCK39 and CCK33) or carboxyl-terminal octapeptide of cholecystokinin (CCK-OP) caused significant increases in outflux of 45Ca, cyclic GMP, and release of amylase. In homogenates of acinar cells each peptide caused a significant increase in adenylate cyclase activity. For each function tested CCK39 was equipotent with CCK33, CCK39 and CCK33 were 10 to 30 times less potent than CCK-OP, the efficacies of CCK39, CCK33, and CCK-OP were the same, and none of these effects were altered by concentrations of atropine sufficient to abolish the action of muscarinic cholinergic agents.

=> log y

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DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-10.58	-10.58

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